Birdsall (W. R.)

A CONTRIBUTION TO THE PATHOLOGICAL ANATOMY OF LEAD PARALYSIS.

BY

W. R. BIRDSALL, M.D.,

Assistant Physician to the Department for Nervous Diseases of the Manhattan Eye and Ear Hospital.

As it is seldom that we have an opportunity to secure an autopsy in cases of lead paralysis, and so few of those made have included an examination of the central nervous system, I feel warranted in presenting the following history of a case, which, though far from being as complete as could be desired, is of sufficient value to be placed on record.

History.—A male, æt. 35, a carriage painter for twenty years, had his first attack of colic in 1871, being sick for three months, during which time he had very marked tremor. One year later, he had a second attack of colic, of four weeks' duration, without paralysis. In 1878, a third attack of colic, of six weeks' duration, supervened with paralysis of the extensors of the wrist and fingers, gradual in its onset, accompanied by pains in the feet and legs so severe that he was unable to walk; also with pain on micturition. Partial recovery followed, slight paresis remaining, and the continuance of the pain to a slight degree. Three months before death (July, 1881), a new attack of paralysis of the extensors of the fingers and wrist occurred, being very slight in the thumbs and index fingers; there were also some dragging of the toes, severe burning pain

in soles of the feet, slight numbness in the fingers, and more or less vertigo, but no colic; no headache.

He had been addicted to the excessive use of alcoholic drinks since youth (of late years only at long intervals); during last illness drank excessively to obtain relief from pain. Occasional epileptiform attacks had occurred since childhood; at times having been six years without an attack, but intervals of six months or a year were more frequent. He had a habit of talking to himself, and at times imagined that he would become insane, but no signs of mental impairment were observed, and his memory was excellent.

The patient was first seen by me at the Department for Nervous Diseases of the Manhattan Eye and Ear Hospital, in July, 1881; he was suffering such intense pain at the time that he was sent home at once without, unfortunately, any electrical examination having been made. He was more comfortable on the next day, but the day following he suddenly fell to the floor unconscious, and remained in a comatose condition for about three hours, when he died without convulsive movements. The autopsy, which was secured with great difficulty, was made twelve hours after death, by my friend, Dr. R. W. Amidon and myself, under such unfavorable circumstances, however, that it was far from being complete. Nothing remarkable was found on examination of the cranial contents, except a decided fulness of the veins. The spinal cord also appeared normal to the naked eye. Specimens of the affected muscles and the corresponding nerves were not secured unfortunately. The intestines appeared normal. The kidneys were small, their capsules adherent, the cortical layer thinner and paler than normal, and in the pelvis of the left kidney was found a small cyst, the size of a hazel-nut, containing a clear fluid. The muscular system was remarkably well developed, even the affected muscles showing but little

atrophy. The brain and 22 cm. of the spinal cord were placed in a solution of potassium bichromate. The former did not harden well, as the weather was hot; portions, however, were saved.

Microscopical examination of sections stained in carmine, and treated according to Clark's method :—The cerebral cortex exhibited a slight increase in capillary vascularity; the walls of the small vessels were thicker than normal; the perivascular spaces dilated to some extent, containing lymphoid elements to a moderate degree. The nerve-cells did not present an abnormal appearance; though dilated pericellular spaces were seen, some containing lymphoid elements. Amyloid bodies were found, and the same vascular changes and slight increase in the number of lymphoid elements in nearly all parts of the brain, including the optic tract and commissure, the latter not exhibiting any degenerated fibres, however. Vessels with thickened walls, distended perivascular spaces, and capillary hemorrhages, to a slight extent, were found in the floor of the fourth ventricle. These changes were most marked, however, from the decussation of the pyramids to the middle of the cervical enlargement, below which point they gradually became less decided. With exception of the changes mentioned, the pons and medulla appeared normal. The alterations in the vessels were most decided in that part of the cord which is normally most vascular, namely, the central gray column, and respecting the height in the cord, at about four cm. below the decussation of the pyramids. At about this region, for a height of nearly two cm., hardening did not take place perfectly in the centre of the cord. It was first regarded as a spot of simple post-mortem softening, but as softening occurred only in this region, where the most decided anatomical changes were found, the increased vascularity and fluidity of this portion probably rendered

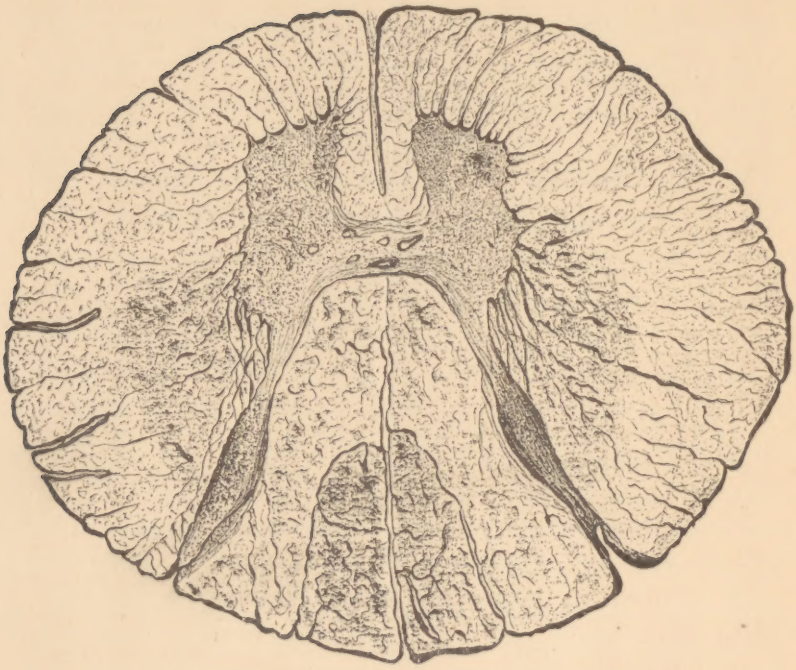

FIG. 1.—Transverse section of cord in the superior cervical region.

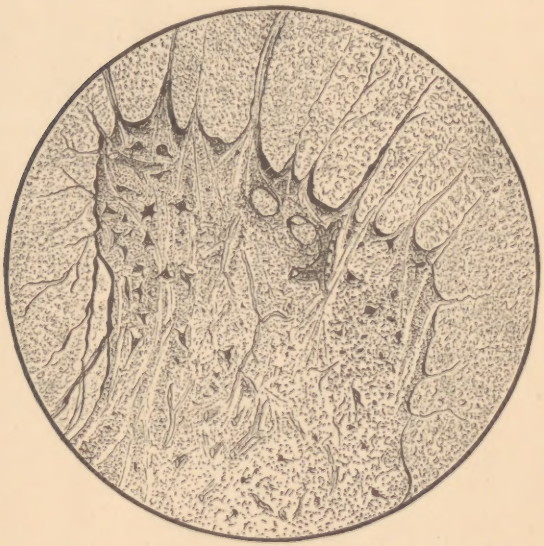

FIG. 2.—Section of anterior horn in the same region more highly magnified.

it more liable to undergo post-mortem changes than the less affected portions The gray matter in this region presented, besides the increased vascularity, many amyloid bodies and an increase in lymphoid elements. Deiters' cells were not abnormally frequent. The nerve-cells of the anterior horns were remarkably well developed in size and number, and a long and careful study of the various cell-groups at different heights of the cervical enenlargement failed to exhibit changes decided enough to warrant the statement that any one group or column of cells were alone affected. The nearest approach to such a condition was found in the outer one of the two peripheric cell-groups in the upper cervical region, at the inner borders of which many of the cells were small and indistinct, and might be considered atrophied or shrunken. A similar appearance, but to a less degree, was found in other cell-groups. The fact that large cells are interspersed with small ones, and that the same column of cells will vary in number and size at successive levels, renders it extremely difficult to conclude, when the changes are not very decided, whether we have a normal or an abnormal condition. It was only the small cells which presented the opposite of these conditions, this being most decided in the neighborhood of dilated vessels or small hemorrhages. The nerve-fibres in the gray matter did not present any decided changes, nor was any decided degeneration positively determined in the anterior roots of the cervical nerves, although increase in the neuroglia along the root-bundles, and in some cases the vascular changes described along their course, would exclude a perfectly normal state. Where the root-bundles were broad, numerous lymphoid bodies were seen between the fibres, and this was particularly well marked in the posterior roots of the cervical region. The white columns presented some thickening of the septa near the gray matter.

The *processus reticularis* and the columns of Goll exhibited a slight degree of sclerosis in excess of the normally greater density of these portions.

Before reviewing the facts in this case, a summary of the results of previous examinations in cases of lead paralysis will prove interesting.

We will exclude the twenty-one cases collected by Tanquerel des Planches[1] in which examinations of the brain were made, also other observations of the older writers which were unaccompanied by a microscopical examination. Nor shall we recite the numerous accounts of examinations of the muscles and nerves, which confirmed the fact that the changes were those of a more or less marked degeneration of the muscle and nerve elements, and their accessory connective-tissue elements, similar to those found after nerve-injury, and after poliomyelitis anterior, more particularly, however, in progressive muscular atrophy, the alterations usually not being very decided. Although the most marked neural changes were found in the intramuscular nerves, yet alterations were also found in the nerve-trunks, and Dejerine[2] traced these changes up to and into the anterior roots. He reported five cases, in three of which parenchymatous neuritis was found in the anterior roots.

Kussmaul and Mayer[3] found, in a case of lead colic, sclerosis of the cortex and superior cervical ganglia, increase of connective tissue, and deformity of the cells; a slight degree of periarteritis was found in the brain and cord, as well as changes in the mucous and muscular coats of the stomach and intestines.

Lancereaux[4] found in two cases atrophic changes in branches of the musculo-spiral nerve, but no change in the nerve-roots, or in the cord. In a third case, however, the patient, æt. 37, had been affected with paralysis of the extensor group of the forearm for ten years, also with

arthralgia and epilepsy; and died from renal cirrhosis. The cord at the cervical enlargement was softer than normal; a number of the ganglion-cells were atrophied or more granular than normal; two roots on the right side above the cervical enlargement were atrophied.

Gombault[6] found no changes either in the brain or cord of a painter with a contracted kidney. The musculo-spiral nerve exhibited changes in the medullary layer and in the connective-tissue elements, but the axis cylinders were preserved.

In Bernhardt's[6] case, in which Westphal[7] made the microscopical examination of the spinal cord with negative results, while he found what he considered degeneration of nerve-fibres in the musculo-spiral nerve, namely: bundles of non-medullated nerves; the patient had been affected with lead paralysis for two years. According to Bernhardt, the spinal dura was covered with spots and streaks, and in the pia of the posterior surface of the lumbar enlargement, calcareous granules were found. He considered the cord smaller and thinner than normal, and reported a variation in the size of the anterior horns in the dorsal region, which was not confirmed by Westphal. The cerebral pia was opaque and œdematous; the vessels were thickened and calcified to some extent.

Tiburtius[8] also arrived at negative results in the examination of the spinal cord in a case of lead paralysis and epilepsy. Changes were found in the muscles, and atrophic changes in the small muscular branches, often extensive. It was claimed that healthy nerves present the same picture which Westphal described.

Vulpian[9] found, in case of lead paralysis of the extensors of the fingers, that the muscles and peripheral nerves were altered, and in the roots of the nerves in the cervical enlargement instances of sclerosis. Some of the cells contained vitreous colloid bodies, and others being of the amy-

loid type. It may be mentioned here, also, that in a dog poisoned by Vulpian with plumbic acetate, in small quantities administered for a considerable time, during which the posterior muscles were first affected, then the anterior, death following; the changes found consisted of subacute myelitis in different regions; nerve-cells were seen in process of destruction, altered nerve-fibres, and great numbers of granular bodies.

[Kast[20] believes that the paralysis which Mason[21] induced in frogs with plumbic acetate was due to the acetic acid, and not to the lead, as controlling experiments with plumbic chloride gave negative results.]

Friedländer [10] reported a case in which there were several attacks of colic and paralysis of the extensor group of the forearm, with absence of electrical excitability during the last attack, which resulted in death from gradual exhaustion. The cord exhibited no changes; except a certain softness, particularly in the cervical region, and a little plate of bone in the arachnoid; great numbers of slender nerve-fibres were found, particularly in the posterior nerve-root; degenerative changes in the muscles and corresponding nerves, and to a less degree in the musculo-spiral nerve.

A case has been reported by Gueneau de Mussy and Lemaire [11] of several attacks of lead colic and paralysis, terminating in convulsions and death, in which a large hemorrhage into the left ventricle was found, and Bramwell [12] reports an autopsy on a worker in lead in which thickening of the frontal bone was found and meningitis principally on the convexity of the cerebrum. It is probable that the lesions found were specific, as the patient had had syphilis.

Eisenlohr [13] reports a case in which the muscles were affected in very different degrees of intensity; those presenting the most decided changes possessing still a recog-

nizable transverse striation in many portions. Accumulations of fat existed at places in the connective tissue, which formed the principal substance. In other muscles, the fibres were partly reduced in size, punctated, moderately pigmented, and the nuclei increased in volume to a marked degree.

In the large nerve-trunks were many exceedingly slender nerve-fibres, a number of which had lost their medullary sheaths. The connective tissue was increased. Neither on the anterior nor posterior roots, nor in the spinal cord, were pathological changes to be found. The author favors the view of a primary lesion of the motor nerves.

Zunker[14] has published the following interesting case. A painter, æt. 36, had had colic ten times from 1865 to 1873, then paralysis of the extensors of the fingers and of the thumb muscles; recovery followed, then a return o the difficulty, again followed by recovery. In 1876, he had colic, complete paralysis of the hands, muscular atrophy in the forearms and hands, paresis of the legs, together with tearing pains, resulting in sufficient improvement for resuming work. In 1878, the paralysis appeared again, at which time an examination revealed paralysis in both forearms, of the musculo-spiral group, excepting the supinators, with atrophy, particularly on the left where even the supinators were slightly involved. The hand remained in a position of decided flexion, the muscles of the thenar and hypothenar groups and the interossei were paralyzed and considerably atrophied. The lower extremities were of diminished size, particularly the extensors. Paralysis of the left extensor digitorum and peronei existed, and on the right paresis of the same. A slight vago-equinus position was present on both sides. No perceptible sensory disturbances were observed. The extensors and hand muscles on both sides failed to react either to

faradism or galvanism, also the extensors and peronei of the left lower extremity; those of the right side showed qualitative changes.

Autopsy: On section of the fresh spinal cord were found clear rounded flakes without recognizable structure in the lateral and anterior columns, particularly near the gray matter.

The whole muscular system, excepting the supinators, presented a pale reddish-brown color. The extensors of the forearm exhibited a firm tendinous tissue, with narrow lines of yellowish-red muscular substance, most marked on the left. In the legs the atrophy was less.

Microscopical examination:—The peroneal nerve exhibited a large quantity of wavy connective tissue, numerous degenerated nerve-fibres. The musculo-spiral, at the point of alteration, exhibited, particularly the left, a great number of degenerated fibres, the greater portion, however, remaining intact; the connective tissue being more scanty than in the peroneus. In both nerves multiplication of the nuclei had taken place. Section of the triceps showed marked degenerative neuritis. The vessels of the nerves possessed very thick walls. At the middle of the forearm, the median and ulnar nerves exhibited a slight increase in the number of nuclei. The extensors of the fingers appeared transformed into a tendinous connective tissue, exhibiting an interstitial fatty accumulation, with here and there collections of cells, the remains of contractile substance. The remaining muscles present changes of a less decided character—namely, a myositis.

The spinal nerve-roots were small, possessed numerous amyloid bodies, but otherwise normal. In the pons, medulla, and cord were numerous amyloid bodies. The flakes described above, stained with hæmatoxylin, osmic acid, and Brunswick brown, but not with carmine. In the lower cervical portion, a line of sclerosis, 3 mm. long,

the size of a pin point, was seen. The anterior horns were reduced in size in their median portions, atrophied, and possessed many amyloid bodies.

The atrophy was most marked from the middle of the dorsal region nearly to the lumbar enlargement. The left anterior horn was transparent, consisting of fine fibres, the ganglion-cells being smaller than on the opposite side, and sometimes failing entirely for long distances. The cells of the lateral horns and of Clark's column were intact. The ganglion-cells of the cervical and lumbar enlargement were not appreciably diminished in number, but of smaller size than normal, as if shrunken; most of them being small and compact. The intra-spinal portions of the anterior root were reduced in size only in the region of the atrophic left anterior horn.

Zunker emphasizes the improbability of the view that the changes extend from the centre to the periphery. The absence of the circumscribed local changes in the cervical and lumbar enlargements, the presence of such changes as compared with those found in the atrophic spina. paralyses in a region the corresponding muscles of which do not seem to have been affected by lead paralysis, leads him to the view that the muscular system and the nerves become affected independently about the same time; other organs, including the spinal cord, becoming involved as the disease becomes general (*Jahresb.*, 1880, 2d Bd., I. Abth., S. 89).

The following is an abstract of Monakow's[15] case:

Male, æt. 56, a painter for forty years, the father of five children, who all died in youth in convulsions; has had repeated attacks of lead colic. Ten years ago had paralysis of the extensors of the right hand, which involved, two years ago, the muscles of the thenar eminence; since then has exhibited signs of psychical impairment of the type of dementia paralytica. Examination reveals blue

line of gums, paresis of the oral portion of the left facial nerve, completely expanded pulse; paresis of the right arm, slight flattening of the right deltoid; disappearance of the right thenar eminence and the extensors of the right forearm; walk slow and difficult; speech slow; articulation indistinct and imperfect; left hemi-analgesia; psychical feebleness. In the later course of the disease, development of exaggerated ideas and maniacal excitement.

Autopsy:—Pachymeningitis externa; hydrocephalus externa; lepto-meningitis chronica, without cortical adherence; atrophy of frontal and central convolutions; hydrocephalus chronica interna; ependymitis chronica. Spinal cord, especially the cervical portion, remarkably small and of less than normal consistence.

Microscopical Examination:—In extensor digitorum communis, in places, normal primitive fibres, with considerable increase in nuclei; others, small, brittle, transversely divided; still others exhibiting fatty degeneration and a moderate growth of connective and fatty tissue. The branches of the musculo-spiral nerve supplying the extensors exhibit only a few normal fibres, the medullary substances showing granular disintegration, the axis cylinder frequently lying free or in wavy connective tissue, rich in cells; in the trunk of the nerve most of the fibres being well preserved. The nearer the cord, the less the changes. The examination of teased preparations of the cervical cord reveals numerous corpora amylacea, decided pigmentation of the ganglion-cells. The hardening of the specimen was not complete. At the level of the sixth cervical vertebra the right anterior horn is reduced one-third; the number of the ganglion-cells diminished, some of them very small, strongly pigmented, and having slender winding processes. The anterior horn exhibits two spaces filled with fine fibrillæ only; somewhat lower, in the region of the middle cell-groups, are numerous spider-

cells and several atrophic ganglion-cells. The anterior group of cells is also atrophic. In the left anterior horn similar atrophic conditions are present. At the level of the eighth nerve, numerous small hemorrhages, vessels with thickened walls rich in nuclei, here and there aneurismal dilatations. At the seventh cervical nerve are spots of disseminated sclerosis, partly located in the posterior horn. The white substance exhibits marked growths of the neuroglia, and here and there patches of sclerosis. The dorsal region of cord is normal. In the lumbar enlargement, small hemorrhages and a few atrophic cells exist. The brain, examined fresh, shows dilated perivascular spaces, filled with lymph-cells, granular corpuscles, and aggregations of pigment, the ganglion-cells being strongly pigmented. Sections from the atrophied convolutions show thinning of the cortex, many free nuclei, and numerous spider-cells; the majority of the ganglion-cells being atrophied. In the white substance are miliary hemorrhages. There is considerable atrophy of the trigeminal nucleus, to a moderate degree of the acoustic, the glosso-pharyngeal, the vagus, and the accessory nucleus; and the hypoglossal nucleus is almost completely atrophied.

Monakow considers the disease due to lead poisoning. The cerebral changes, he points out, are almost identical with those of progressive paralysis of the insane (*Jahresb.*, 1880, 2d Bd., 1. Abt., p. 89).

Dr. S. Moritz,[*] of Manchester, England, reported a case of a glass founder, who died from uræmia six weeks after an attack of paralysis of the extensors of the forearm. The extension of the right hand was impossible, while the left side was less affected. "The muscles were somewhat soft and flabby, but did not appear particularly wasted."

On microscopical examination by Drs. Dreschfield and

Young, the kidney showed a chronic interstitial nephritis The cervical cord showed no abnormalities whatever; but. in the musculo-spiral nerve degenerative changes were found, and the muscles exhibited changes similar to those found by Friedreich in progressive muscular atrophy. The author favors the view that the changes in the muscles were secondary to those in the nerves. The case is well reported. Monakow's and Moritz's papers give the most complete reviews of the subject that have appeared.

In addition to these cases, which are all I have been able to find in the literature of the subject at my command of examination of the spinal cord in lead paralysis, I am informed by my friend, Dr. E. C. Seguin, that in 1874 he reported at the Society of Neurology and Electricity the results of a microscopical examination of the spinal cord, the nerves, and muscles in a case which had partially recovered from lead paralysis of the extensor group of the forearm. He found, aside from slight changes in the muscles and nerves, a slight reduction in the size and number of the cells of the anterior horns in the cervical region, with occasional signs of degeneration in certain cells. From the specimens which he kindly loaned me for examination, I was able to confirm his statements, but the changes were too slight, as in my own case, to localize the lesion positively in any one group of cells. This case has never been published that I can ascertain.

The complications with other diseased conditions, in some of the cases presented, raises the question whether the lesion found might not have been due to other causes than chronic lead poisoning; and my own case is open to the same objection, as the lesions found resemble those observed in cases of epilepsy and of chronic alcoholism to a considerable extent. The predominance, however, of the alterations described in the cervical cord at the origin of the nerves supplied to the affected muscles argues against

this view. We think we are justified in concluding that a mild grade of subacute myelitis existed in this case, not sufficiently marked to show very decided changes in the nerve-cells, but which might still be sufficient to impair their functions.

Out of the fourteen cases here mentioned, in which the spinal cord was examined, in six of them (Lancereaux, Vulpian, Zunker, Monakow, Seguin, Birdsall) changes were found to a greater or less degree, and changes similar in character. Such a large percentage of positive cases outweighs the negative ones in favor of involvement of the cord in lead paralysis, but it does not settle the question whether the cord is primarily, secondarily, or simultaneously involved in relation to the muscles and peripheral nerves. The fact that changes have been noticed in the muscles and muscular nerve branches before they could be detected in the cord is not a conclusive argument against the theory of a central origin of the changes. Impairment of function in the spinal centres is more liable to affect the nutrition of centrifugal nerves and organs than the latter are to react upon the former, as long as Waller's law holds true.

The chemical experiments which show that the spinal cord retains relatively more lead than any other of the parts except the bones,[17] are in favor of a central origin of the disease, as are also the clinical facts when compared with clinically allied diseases known to be associated with anatomical alterations in the cord. As it is not the purpose of this article to discuss at length the pathology of lead paralysis, but to summarize the pathological findings, we must conclude with the statement that many more cases are required to decide this question positively, and to settle the theoretical questions first thoroughly agitated by Remak,[18] concerning the localization of functions in

different heights and different cell-groups of the cord, the material which we now have is of but little avail.

The renal lesions found in our case were evidently the cause of death, as they have been in so many other cases —a fact to which Lancereaux[10] in particular has called attention. Although requested, a specimen of the urine was not obtained before his death, and an unpleasant interference at the autopsy resulted in our not securing the kidneys for microscopical examination. The lesions were evident to the naked eye, however. While the attack, which resulted in his death, was probably uræmic, the epileptic attacks, to which he had been occasionally subject, began in infancy, hence could not have been the result of chronic lead poisoning; the latter factor may have proved an exciting cause, however.

BIBLIOGRAPHY.

[1] Tanquerel des Planches.—Traité des maladies du plomb. Paris, 1839.

[2] Déjérine.—Recherches sur les lésions du système nerveux dans la paralysie saturnine. *Gaz. Méd. de Paris*, 1879, 12.

[3] Kussmaul and Mayer.—Zur path. Anat. des chron. Saturnismus. *Deutsch. Arch. f. klin. Med.*, Bd. VIII.

[4] Lancereaux.—Note relative à un cas de paralysie saturnine avec altérations des cordons nerveux et des muscles paralysé. *Gaz. méd. de Paris*, 1862, No. 26.

Ibid.—Saturnisme chronique avec accès de goutte et arthritis, etc. *Gaz. méd. de Paris*, 1862, p. 707; 1871, p. 383.

[5] Gombault.—Contribution à l'histoire anatomique de l'atrophie musculaire saturnine. *Arch. d. physiol. norm. et path.*, V., 1873.

[6] Bernhardt.—Zur Pathologie der Radialisparalysen. *Arch. f. Psych. u. N.*, Bd. IV., Heft III., S. 601.

[7] Westphal.—Ueber eine Veränderung des N. radialis bei Bleilähmung. *Arch. f. Psych. u. N.*, Bd. IV., S. 776.

[8] Tiburtius.—Die Extensorenlähmung bei chron. Bleivergiftung. *Inaugural Dissertation*, Zurich, 1876 (see also 6, 15).

[9] Vulpian.—Maladies du système nerveaux. Paris, 1879, p. 158.

[10] Friedlander.—Anatomische Untersuch. eines Falles von Bleilähmung. *Virch. Arch.*, Bd. 75, H. 7, 1879.

[11] Guéneau de Mussy and Lemaire.—Arthralgie saturnine, etc. *Gaz. des Hôp.*, 1863, No. 82.

[12] Bramwell.—The differential Diagnosis of Lead Encephalopathy, etc. *Edinb. Med. Jour.*, December, 1879.

[13] Eisenlohr.—Ein Fall von Bleilähmung, etc. *Deutsch. Arch. f. clin. Med.*, Bd. 26.

[14] Zunker.—Zur Pathologie d. Bleilähmung. *Zeitschrift f. clin. Med.*, 1880, I., 496.

[15] Monakow.—Zur pathologischen Anat. der Bleilähmung, etc. *Arch. f. Psych. u. N.*, Bd. X., H. 2.

[16] Moritz.—Pathological Anatomy of Lead Paralysis. *Jour. Anat. and Phys.* London, October, 1880.

[17] Heubel.—Pathogenese u. Symptome der chronischen Bleivergiftung. Berlin, 1871.

[18] Remak.—Zur Pathogenese der Bleilähmung. *Arch. f. Psych. u. N.*, Bd. VI., H. 7.

[19] Lancereaux.—De l'Alteration des reins dans l'intoxication saturnine. *Union. Méd.*, No. 150, 1863.

[20] Kast.—Notizen zur Bleilähmung. *Centralbl. f. Nervenheilkunde*, etc., No. 8, 1880.

[21] Mason.—Lead Poisoning in Frogs. *New York Med. Jour.*, July, 1877.